Deficits in Facial Emotion Recognition in Patients with Epilepsy: Comprehensive Understanding from Cognitive Neuroscience Perspectives

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Abstract: Facial emotion recognition is a key aspect of social cognition, crucial for social interactions. Recent studies have focused on deficits in facial emotion recognition among patients with epilepsy (PWE) and the factors influencing these deficits. Research suggests that brain damage caused by epilepsy may lead to specific impairments in recognizing emotions, with lateralization of epilepsy and the emotional intensity of stimuli playing important roles. Additionally, interactions between emotion type, emotional intensity, and the age of onset of epilepsy may contribute to these recognition deficits. Different treatments for epilepsy may have varying effects on facial emotion recognition. However, the precise mechanisms and the extent to which these epilepsy-related factors and stimulus variables contribute to these deficits remain unclear. To solve these problems, we introduced the effects of epilepsy type, lateralization, and age of onset on facial emotion recognition abilities, and explored the underlying mechanisms from a cognitive perspective. Future research should experimentally test these mechanisms, considering different ages of epilepsy onset and levels of emotional intensity. This would provide theoretical support for interventions aimed at mitigating emotion recognition deficits in PWE.

Keywords: Epilepsy; Facial emotion recognition; Neural mechanisms

"In the case of Dr. P, his difficulty was not in seeing, but in making sense of what he saw. He could not recognize the face of his wife, whom he had been married to for many years. Instead, he saw her face as an object, a mere collection of features, and was unable to integrate them into a meaningful whole."

—— Oliver Sacks, *The Man Who Mistook His Wife for a Hat* (1985)

1. Introduction

Dr. P's case highlights the importance of the relative position of facial features in facial identity recognition (Maurer et al., 2002). In addition to identity detection, facial recognition also involves interpreting facial features to identify emotional states (Ekman & Friesen, 2003; Callahan et al., 2011; Stewart et al., 2019). Mirror neurons play a crucial role in this process, helping to capture and process emotional information, which triggers psychological and physiological responses that influence social behavior (Van Overwalle, 2009). Accurately recognizing facial emotions and responding appropriately aids in building effective interpersonal relationships (Keltner et al., 2003), while deficits in facial emotion recognition can reduce peer interactions and increase psychological and social stress (Frith & Frith, 1999; Yeates et al., 2007).

Investigating the effects of brain damage on specific cognitive functions helps establish the connection between brain structure and cognition, providing a foundation for understanding cognitive mechanisms in the brain. Early neuropsychological research on brain-injured patients revealed the specific functions of different brain regions. For example, the discovery of Broca's area and Wernicke's area highlighted the importance of specific brain regions in language processing (Broca, 1861; Wernicke, 1874). Studies on brain-injured patients not only deepened our understanding of various cognitive functions, such as language, memory, and emotion, but also contributed to the development of brain function networks. Gazzaniga and Sperry (1967), through their study of split-brain patients (patients with severe epilepsy who underwent corpus callosotomy), revealed the differences between the left and right hemispheres in language processing.

Epilepsy is a chronic neurological disorder characterized by recurrent seizures without a clear trigger (Fisher et al., 2014). It affects approximately 50 million people worldwide (over 0.5% of the global population), with more than 5 million new cases annually (World Health Organization, 2024). Epilepsy can be classified into focal epilepsy and generalized epilepsy based on the type of seizure (Scheffer et al., 2017). Generalized epilepsy has no identifiable lesion or brain structure abnormalities, while focal epilepsy (e.g., temporal lobe epilepsy) typically originates in one hemisphere and is closely related to acquired lesions, tumors, or congenital brain structural abnormalities (Fisher et al., 2014). Several review articles have highlighted facial emotion recognition deficits in patients with focal epilepsy (e.g., Monti & Meletti, 2015; Edwards et al., 2017; Witt & Helmstaedter, 2017), and seizures may affect the function of multiple brain regions (Fisher et al., 2014). Thus, studying facial emotion recognition deficits in PWE helps advance our understanding of the neural mechanisms of facial emotion recognition. Given that epilepsy often begins in childhood and persists into adulthood (Byars et al., 2014), and that emotion recognition abilities mature with age

(Herba & Phillips, 2004), investigating the effects of epilepsy at different developmental stages could deepen our understanding of the developmental process of facial emotion recognition.

Despite the growing research on facial emotion recognition deficits in PWE in recent years, the effects of epilepsy variables (e.g., lesion location and antiepileptic drugs) and stimulus variables (such as emotion type and emotional intensity) on facial emotion recognition deficits remain unclear. For example, the impact of epilepsy on specific facial emotions is still inconclusive. While most studies have found deficits in recognizing facial fear in PWE (e.g., Farrant et al., 2005; Benuzzi et al., 2014; Rainer et al., 2023), some studies showed inconsistent findings (e.g., Yamada et al., 2005; Realmuto et al., 2015). Additionally, it is still unclear to what extent the treatment methods affect facial emotion recognition deficits in PWE. Therefore, this review aims to integrate existing research to clarify the influence of epilepsy and stimulus variables on facial emotion recognition. Building on this foundation, it further explores the specific mechanisms through which different factors affect facial emotion recognition in PWE from a cognitive process perspective. Given that the number of patients with occipital lobe epilepsy is small (Angus-Leppan & Clay, 2021) and their seizures may cause functional and structural abnormalities in the occipital visual cortex, severely affecting visual processing, this review does not include patients with occipital lobe epilepsy.

2. Cognitive Neuroscience Framework for Facial Emotion Recognition

Emotions are a fundamental part of human life (LeDoux et al., 2016) and play a crucial role in human development and the progression of mental disorders. Understanding the cognitive mechanisms of facial emotion recognition helps to reveal the specific roles of epilepsy variables and stimulus variables in the recognition process of PWE. The Basic Emotion Theory is one of the classic theories in emotion research (Ekman, 1992, 1999; Ekman & Davidson, 1994; Scarantino & Griffiths, 2011; Hutto et al., 2018). This theory suggests that emotions can be divided into a limited number of discrete categories. The most common classification is the six basic emotions proposed by Ekman et al. (1992) based on typical facial emotion images: happiness, anger, fear, sadness, disgust, and surprise.

Each basic emotion has unique physiological manifestations and distinct neural bases (citations). For example, smile is a physiological manifestation of happiness, while anger is associated with furrowed brows (Ekman, 1993). Regarding distinct neural bases of emotions, neuroimaging studies have identified specific brain nuclei

responsible for processing certain emotions. For instance, disgust triggers persistent activation in the insular region (Wright et al., 2004), while fear evokes responses in the amygdala (Vuilleumier, 2005).

However, in addition to these nuclei, other regions are typically involved in the perception, evaluation, or regulation of emotions (Phan et al., 2002; Lindquist et al., 2012, 2013; Gu et al., 2019). The Psychological Constructionist Theory further suggests that facial emotion recognition results from the collaboration of multiple brain regions (Barrett & Bliss-Moreau, 2009; Lindquist et al., 2012). Studies have shown that happiness activates a broad range of brain regions, including the rostral anterior cingulate cortex, right superior temporal gyrus, prefrontal cortex, insula, and hippocampus (Vytal & Hamann, 2010; Suardi et al., 2016; Kluczniok et al., 2017). Besides, Gu et al. (2019b) suggests the ventral tegmental area indirectly participates in the cognitive processing of happiness by releasing dopamine to the locus coeruleus, prefrontal cortex, and anterior cingulate cortex. In fear processing, the amygdala plays a major role (Vuilleumier, 2005), but regions such as the hippocampus and anterior cingulate cortex are also involved (Britton et al., 2006). Emotions such as anger, disgust, and sadness similarly rely on the collaborative processing of multiple brain regions (Britton et al., 2006; Lindquist et al., 2012; Gu et al., 2019).

Facial emotion recognition is a complex cognitive process that depends on the collaboration of cortical and subcortical pathways (LeDoux, 1996; Adolphs, 2002b; Leppänen & Nelson, 2006; Pessoa & Adolphs, 2010). The cortical pathway is responsible for the fine processing of emotional information and is the primary route for facial emotion recognition, while the subcortical pathway supports rapid responses to emotionally significant stimuli. The developmental trajectories of these pathways differ: the subcortical pathway matures earlier, whereas the cortical pathway has a longer developmental period; additionally, the subcortical pathway is less influenced by social experience compared to the cortical pathway; furthermore, the cortical pathway is associated with the gradual improvement in the specificity of related brain regions, a characteristic not observed in the subcortical pathway. In addition, facial emotion recognition relies on the coordinated action of multiple brain regions, including the fusiform gyrus (Kawasaki et al., 2012), superior temporal sulcus (Said et al., 2010), amygdala (Herrington et al., 2011), insula (Boucher et al., 2015), and anterior cingulate cortex (Fan et al., 2011), to implement at least two key mechanisms: (1) simulating the observer's emotional experience, and (2) modulating the sensory cortex through top-down regulation (Adolphs, 2002b; Wood et al., 2016; Richey et al., 2022).

The cognitive process of facial emotion recognition can be divided into three main stages: the processing of basic facial features, the processing of emotional features, and feedback regulation (Adolphs, 2002b). In the basic facial feature processing stage, facial emotional stimuli are processed at a low level by the Occipital Face Area (OFA)

in the occipital lobe. Functional magnetic resonance imaging (fMRI) and transcranial magnetic stimulation (TMS) studies show that early in visual processing, the OFA prioritizes representation of parts such as the nose and eyes (Pitcher et al., 2009; Liu et al., 2010; Pitcher et al., 2011). Pitcher et al. (2009) used TMS to stimulate the right OFA, selectively affecting facial recognition performance without significantly impacting object recognition. This information is then transmitted via the cortical pathway to the fusiform gyrus and superior temporal sulcus for the initial extraction of identity and emotional features (Leppänen & Nelson, 2006; Blank et al., 2015). Using fMRI and support vector machine pattern classification analysis, Zhang et al. (2016) found that the superior temporal sulcus is more sensitive in distinguishing emotional faces from neutral ones, while the fusiform gyrus is more sensitive to distinguishing facial identity. After processing basic facial features, the amygdala and orbitofrontal cortex allocate attention based on the correlation between facial information and emotional features, beginning the processing of emotional features (Adolphs, 2002b; Leppänen & Nelson, 2009; Richey et al., 2022). The amygdala and orbitofrontal cortex, through functional connectivity with the dorsolateral prefrontal cortex and hippocampus, extract emotion-related memory representations to more accurately differentiate emotion types (Bar, 2003; Anderson et al., 2016). The amygdala is involved not only in the fine processing of facial emotions but also in regulating alertness, which influences the processing of sensory information (Leppänen & Nelson, 2006). Its functional connection with the basal forebrain structures promotes acetylcholine release, increases sensory cortical activation, and speeds up cognitive processing, helping individuals make rapid responses. Liu et al. (2021), through meta-analytic connectivity modeling (MACM), integrated 96 fMRI and positron emission tomography (PET) studies and similarly found that facial emotion recognition results from the coordinated action of brain regions such as the amygdala, superior temporal sulcus, and fusiform gyrus.

Several reviews have systematically summarized the facial emotion recognition deficits and influencing factors in PWE (Monti & Meletti, 2015; Bora & Meletti, 2016; Edwards et al., 2017; Mikula et al., 2021; Qi et al., 2022; Ziaei et al., 2023). However, these studies mainly focus on the specific manifestations of facial emotion recognition deficits in PWE and the relationship between damage to specific brain regions and these deficits (Monti & Meletti, 2015; Qi et al., 2022; Ziaei et al., 2023). Few have systematically addressed how epilepsy-related and stimulus-related factors affect the facial emotion recognition process. Therefore, this review aims to summarize the cognitive process and corresponding mechanisms of facial emotion recognition and further explore how epilepsy variables and stimulus factors impact the facial emotion recognition process in PWE.

3. Where Epilepsy Strikes: Mapping Lesion Location to Emotion Recognition

This review first explores the specific effects of epilepsy lesion locations on the recognition deficits of different facial emotions. Overall, both focal epilepsy patients (Farrant et al., 2005; Tanaka et al., 2013) and generalized epilepsy patients (Gomez-Ibañez et al., 2014; Rainer et al., 2023) show significantly lower facial emotion recognition abilities compared to healthy individuals. Most of the research focuses on temporal lobe epilepsy (TLE), the most common type of epilepsy, with fewer studies on frontal lobe epilepsy (FLE). These studies primarily indicate that patients with FLE may have difficulty in recognizing emotions such as fear (Farrant et al., 2005; Laurent et al., 2014; Rainer et al., 2023), sadness (Meletti et al., 2003), and disgust (Tanaka et al., 2013). Additionally, Banks et al. (2014) found that patients with TLE also exhibit significant deficits in recognizing neutral faces.

As a core component of the "emotion brain" (Bickart et al., 2014), the amygdala is closely associated with facial fear recognition deficits in PWE. The two-streams hypothesis of visual processing (Mishkin & Ungerleider, 1982) posits that humans possess two visual pathways: the ventral pathway and the dorsal pathway. Once visual information leaves the occipital lobe, the ventral pathway is involved in recognizing shape, color, and other information, while the dorsal pathway processes spatial information. The amygdala is functionally linked to the fusiform face area (FFA), a key part of the ventral pathway, and regulates attention to emotional stimuli through the fusiform and occipital cortices (Anderson & Phelps, 2001; Vuilleumier et al., 2004). In addition, it integrates visual input from the thalamic occipital region (Cotton & Smith, 2007), further contributing to the processing of emotional stimuli. Therefore, amygdala damage caused by epilepsy (especially damage to the uncus, Dilger et al., 2003) may weaken this functional connectivity, affecting the recognition process of fearful faces (Vuilleumier, 2005). Furthermore, the amygdala plays a regulatory role in the integration of emotional memories (Phelps & LeDoux, 2005). Through connections with the hippocampus and prefrontal cortex, the amygdala helps establish links between emotional information and emotional memories to trigger adaptive emotional responses (Adolphs, 2002a). Thus, amygdala damage caused by epilepsy may interfere with the integration of facial emotional information and the retrieval of emotional memories, exacerbating various facial emotion recognition deficits in PWE, particularly in those with temporal lobe epilepsy (Tanaka et al., 2013; Benuzzi et al., 2014).

Different epileptic focus regions may lead to variations in facial emotion recognition

abilities among PWE. For instance, temporal lobe epilepsy primarily involves deficits in fear emotion recognition (Meletti et al., 2003; Tanaka et al., 2013; Benuzzi et al., 2014), while patients with frontal lobe epilepsy may experience difficulties in both fear and anger emotion recognition (Farrant et al., 2005; LeDoux, 2003; Pessoa, 2017). Regarding anger, the orbitofrontal cortex and medial prefrontal cortex are both involved in the processing of anger (Adolphs, 2002a; Gu et al., 2019). Therefore, functional abnormalities in the orbitofrontal cortex and medial prefrontal cortex induced by epilepsy may directly affect patients' ability to recognize angry faces. Additionally, medial temporal lobe seizures often lead to functional and structural abnormalities in the orbitofrontal cortex (Lieb et al., 1991), further exacerbating difficulties in recognizing angry faces among PWE. Since the amygdala plays an important regulatory role in the integration of facial emotional information and the retrieval of emotional memories, damage to the amygdala may also affect PWE' recognition of angry faces. These findings suggest that damage to key brain regions involved in facial emotion recognition due to epilepsy may impact the recognition of multiple emotions.

4. The Hemispheric Divide: Impact of Epilepsy Lateralization on Emotion Recognition

Previous studies have found that the lateralization of epilepsy also affects the facial emotion recognition and processing in temporal lobe epilepsy patients. For example, left temporal lobe epilepsy patients do not significantly differ from healthy individuals in recognizing fearful faces (Shaw et al., 2007; Sedda et al., 2013), whereas right temporal lobe epilepsy patients perform significantly worse than both healthy individuals and left temporal lobe epilepsy patients (Meletti et al., 2003; Benuzzi et al., 2014). This result is consistent with the right-hemisphere model (RHM), which suggests that the two hemispheres play different roles in facial emotion processing, with the right hemisphere dominating the perception, experience, and expression of emotions (Borod et al., 1983; Wager et al., 2003). When facing emotional stimuli, the right amygdala is automatically activated and performs the initial processing, while the left amygdala is involved in subsequent more refined processing (Adolphs, 2002b; Glascher et al., 2004; Gainotti, 2012). However, because the right hemisphere has a subcortical fast pathway for emotion processing (Gainotti, 2012), under certain conditions, the right amygdala can compensate for the left amygdala in performing refined processing (Meletti et al., 2003; Sedda et al., 2013). Therefore, when seizures occur in the right hemisphere, patients' emotion recognition ability is more severely

affected (Meletti et al., 2009). However, some studies suggest that there is no significant difference in facial fear emotion recognition ability between PWE and healthy individuals (Banks et al., 2014; Realmuto et al., 2015). One main problem is that these studies did not consider the potential impact of lateralization on the results.

Emotional intensity plays an important role in the lateralization differences observed in temporal lobe epilepsy patients. The dual-pathway theory of emotion processing posits that emotional processing occurs through two pathways: the subcortical pathway and the cortical pathway (LeDoux, 1996; Leppänen & Nelson, 2006; Pessoa & Adolphs, 2010). When faced with high-intensity emotional stimuli, the stimulus information is primarily transmitted through the subcortical pathway via the thalamus to the amygdala, rapidly triggering physiological responses such as increased heart rate and muscle tension, but with lower levels of processing precision. In contrast, when faced with low-intensity emotional stimuli, the information is first processed in the cortex before being passed to brain regions such as the amygdala for more refined processing, resulting in slower but more precise processing (Adolphs, 2002b). The role of emotional intensity in facial emotion recognition may be related to the affective-salience network (ASN), which consists of the amygdala, ventromedial prefrontal cortex, medial orbitofrontal cortex, and dorsal anterior cingulate cortex, among other brain regions (Adolphs, 2002a; Hiser & Koenigs, 2018; Piretti et al., 2022) and has a significant impact on emotional processing. Metzger et al. (2023) found that the affective-salience network is more sensitive to emotional intensity than to emotional valence. For example, in facial emotion recognition, emotional intensity may alter the activation level of the amygdala, influencing the selection of emotional processing pathways (Bonnet et al., 2015). When the intensity of an emotional face is high, amygdala activation increases, and individuals tend to process the emotion quickly through the subcortical pathway; when the intensity of the emotional face is low, amygdala activation is lower, and individuals engage the cortical pathway for more detailed processing.

In groups of TLE patients with different lateralization characteristics, emotional processing pathways may be affected to varying degrees. Sedda et al. (2013) used Morph technology to create facial images with different emotional intensities (35%, 50%, 75%, 100%) to investigate the emotional recognition ability of TLE patients. The results showed that when the emotional intensity was as low as 35% or 50%, right TLE patients performed worse than left TLE patients in overall facial emotion recognition ability and in the recognition of individual emotions (happiness, anger, fear, disgust, sadness). However, when the emotional intensity increased to 75%, the two groups only showed a significant difference in overall facial emotion recognition ability. This suggests that epilepsy negatively affects emotional processing pathways, with the cortical pathway being more severely damaged in right TLE patients. These functional and structural abnormalities in the brain regions caused by epilepsy impact the function

of the affective-salience network, leading to a decline in facial emotion recognition ability. However, fewer studies have focused on the impact of lateralization and emotional intensity on facial emotion recognition ability in other focal epilepsy patients (e.g., FLE patients) and generalized epilepsy patients (e.g., genetic generalized epilepsy patients).

5. Beyond the Lesion: Influence of Antiepileptic Drugs and Surgical Interventions

Besides the aforementioned factors, the types of antiepileptic drugs (AEDs) taken by PWE can also significantly affect their facial emotion recognition ability. Meletti et al. (2009) analyzed the impact of different antiepileptic drugs on facial emotion recognition in TLE patients. The results indicated that most antiepileptic drugs (such as Carbamazepine, Topiramate, Phenytoin, Lamotrigine, Levetiracetam, Clobazam, and Valproate) did not significantly affect facial emotion recognition ability. However, TLE patients taking Phenobarbital showed poorer performance in facial emotion recognition, particularly in recognizing happiness, sadness, and disgust. Phenobarbital is a commonly used antiepileptic drug (Yasiry & Shorvon, 2012) that inhibits abnormal excitation in the central nervous system by enhancing the activity of gamma-aminobutyric acid (GABA) receptors (Suddock et al., 2024). Long-term use of Phenobarbital may lead to adverse effects such as drowsiness, central nervous system depression, and anxiety (Suddock et al., 2024), which can impair cognitive processing, such as facial emotion recognition. Additionally, Phenobarbital may interfere with normal cognitive development, potentially adversely affecting the development of facial emotion recognition abilities in infants (Camfield et al., 1979). Although antiepileptic drugs may influence the cognitive abilities of PWE (Hirsch et al., 2003; Meletti et al., 2009), fewer studies have focused on the role of this kind of drugs in the impact of epilepsy on emotional recognition abilities.

Another factor that may affect the recovery of facial emotion recognition ability in patients is epilepsy surgery. For instance, anterior temporal lobe resection and selective amygdalohippocampectomy may reduce the patient's ability to recognize fear or disgust, whereas stereotactic laser thermocoagulation does not have this effect (Drane et al., 2015). This difference may be related to the degree of neural fiber damage caused by different surgical methods (resective surgery vs. stereotactic surgery). In primates, the amygdala and hippocampus are located deep within the medial anterior temporal lobe. Puncturing or resecting the amygdala or hippocampus

typically damages the surrounding cortex and its neural fiber connections with other brain regions, whereas stereotactic surgery avoids damaging these neural fiber pathways (Easton & Emery, 2005). Yet, existing research has not reached consistent findings in the role of epilepsy surgery in PWE's facial emotion recognition ability. Most studies have not found a significant recovery effect on facial emotion recognition ability following TLE surgery (e.g., anterior temporal lobe resections and selective amygdalohippocampectomy) (Monti & Meletti, 2015; Mikula et al., 2021). However, a few studies suggest that facial emotion recognition ability in PWE improves after temporal lobe surgery (Yamada et al., 2005; Shaw et al., 2007; Benuzzi et al., 2014). Inconsistent results may be due to different comparison groups. Most studies compare postoperative groups with preoperative groups or healthy controls in terms of facial emotion recognition ability, finding that epilepsy surgery did not significantly improve this ability (Anderson et al., 2000; Cohn et al., 2015). However, a few longitudinal studies have compared the pre- and post-surgery facial emotion recognition abilities of the same patient group, finding that epilepsy surgery can help improve patients' facial emotion recognition ability. For example, Benuzzi et al. (2014) found that the fear recognition ability of early-onset right TLE patients significantly improved post-surgery, and that post-surgery patients activated the same brain regions (left orbital frontal cortex and bilateral striatum) as healthy individuals when recognizing fear. Although these studies provide preliminary evidence, the reliability of the results still needs to be carefully evaluated due to the limited number of related studies and small sample sizes.

6. Age of Epilepsy Onset Shapes the Trajectory of Emotion Recognition

Since the development of facial emotion recognition ability begins in the early stages of an individual's life (Walpole et al., 2008), and different facial emotion recognition abilities have distinct developmental trajectories, epilepsy seizures occurring at different developmental stages may have varying degrees of impact on an individual's facial emotion recognition ability. Developmental psychology research shows that the ability to recognize different facial emotions follows different developmental trajectories (Lawrence et al., 2015). This difference is first reflected in the maturity of the recognition ability for different facial emotions, which is closely related to brain development. The recognition of happiness relies on the earlier-developing left amygdala and occipital lobe areas (Herba & Phillips, 2004), so the ability to recognize

happiness in 5-year-old children is close to adult levels (Gao & Maurer, 2009). In contrast, the recognition of negative emotions such as anger, depends on brain regions that continue to develop, such as the left occipital-temporal junction, anterior insula, orbitofrontal cortex, and medial frontal gyrus (Thomas et al., 2007). This leads to the delayed maturation of the ability to recognize negative emotion faces, such as anger and fear (Durand et al., 2007; Broeren et al., 2011; Chronaki et al., 2015; Rodger et al., 2015; Stewart et al., 2019). Additionally, the developmental trends of recognition abilities for different emotions also vary. The ability to recognize happiness and fear increases linearly with age, while the ability to recognize anger experiences a sharp increase during adolescence to adulthood (Thomas et al., 2007). At the same time, individuals' ability to recognize facial emotions of varying intensities also develops differently. Unlike high-intensity (100%) facial emotions, individuals' ability to recognize low-intensity facial emotions improves with age (Ammerlaan et al., 2008; Gosselin et al., 2011; Sedda et al., 2013).

Edwards et al. (2017) found a significant positive correlation between the age of onset of epilepsy and performance on facial emotion recognition tasks in patients with temporal lobe epilepsy. Similarly, Qi et al. (2022) reached a similar conclusion through a meta-regression analysis. In addition, the lateralization characteristics of TLE may interact with the age of onset, jointly affecting the emotional recognition abilities of children and adolescents with epilepsy. The "early-onset" hypothesis suggests that patients with TLE who suffer damage to the right amygdala before the age of 6 will face permanent deficits in facial emotion recognition, while epilepsy with a later onset is less likely to affect facial emotion recognition abilities (Meletti et al., 2003; Hlobil et al., 2008). In generalized epilepsy patients, there is also a close relationship between the age of onset and facial emotion recognition ability (Reynders et al., 2005; Meletti et al., 2009). Accurate recognition of facial emotions requires the effective integration and transmission of emotional information by multiple neural structures (Cristinzio et al., 2010). However, an earlier onset of epilepsy may affect the development of these neural structures and reduce the efficiency of information transmission between them, leading to more severe facial emotion recognition deficits in patients with early-onset epilepsy. According to the dual-pathway theory of facial emotion recognition, the development of the cortical pathway and the enhancement of specific brain areas depends on the accumulation of social experiences (Leppänen & Nelson, 2006). Epileptic seizures are often associated with feelings of shame (Fiest et al., 2014), leading individuals to avoid social interactions, which in turn affects the acquisition of experience related to facial emotion recognition. It is worth noting that although early-onset epilepsy severely impacts facial emotion recognition abilities and may persist for life, most current studies focus on adult PWE, with fewer studies examining the impact of epilepsy on facial emotion recognition abilities in children and adolescents.

7. Discussion

Existing research has reviewed facial emotion recognition deficits in PWE and their influencing factors (Monti & Meletti, 2015; Bora & Meletti, 2016; Edwards et al., 2017; Mikula et al., 2021; Qi et al., 2022; Ziaei et al., 2023). However, these reviews have primarily focused on the association between deficits in specific brain regions (e.g., hippocampus, amygdala) and facial emotion recognition deficits in PWE (Monti & Meletti, 2015; Qi et al., 2022; Ziaei et al., 2023). They have lacked a systematic exploration of how epilepsy-related variables and stimulus-related variables interact to influence the facial emotion recognition mechanisms in patients. Therefore, this review aims to build upon past theoretical and empirical research and systematically explore the mechanisms through which various epilepsy and stimulus-related variables impact facial emotion recognition abilities in PWE.

7.1. An Integrating Model of Impaired Emotion Recognition in Epilepsy

This review is based on the dual-pathway theory of facial emotion recognition (Leppänen & Nelson, 2006), constructing a dual-pathway, three-stage neural network mechanism for facial emotion recognition. Specifically, facial emotion recognition is achieved through cortical and subcortical pathways in three processing stages: basic facial feature processing, facial emotion feature processing, and feedback regulation.

In the basic facial feature processing stage, the occipital facial region prioritizes the representation of basic facial features (Pitcher et al., 2009; Liu et al., 2010; Pitcher et al., 2011), and this information is transmitted through the cortical pathway to the fusiform gyrus and superior temporal sulcus to initially extract identity and emotional features of the face (Leppänen & Nelson, 2006; Blank et al., 2015; Zhang et al., 2016).

In the facial emotion feature processing stage, regions such as the amygdala and orbitofrontal cortex allocate attention according to emotional features and their relevance to emotions and process them in more detail (Leppänen & Nelson, 2009; Richey et al., 2022). Moreover, through functional connectivity with the dorsolateral prefrontal cortex and hippocampus, the amygdala and orbitofrontal cortex also participate in extracting emotion-related memories, enabling more accurate differentiation of emotion types (Bar, 2003; Anderson et al., 2016). In addition, while the amygdala processes facial emotions, it also influences sensory cortical processing by regulating alertness levels, promoting faster responses to emotional stimuli

(Leppänen & Nelson, 2006).

The amygdala, orbitofrontal cortex, and other regions play important roles in the facial emotion feature processing stage. However, epilepsy seizures can lead to structural and functional abnormalities in these areas, affecting the facial emotion recognition process in PWE. For example, structural and functional abnormalities in the amygdala due to seizures can impair an individual's attention to emotional stimuli (Anderson & Phelps, 2001; Vuilleumier et al., 2004; Cotton & Smith, 2007), memory retrieval related to emotions (Adolphs, 2002b; Phelps & LeDoux, 2005), and weaken the functional connectivity between the amygdala and fusiform gyrus, thus affecting feedback regulation on the sensory cortex (Leppänen & Nelson, 2006). Moreover, seizures can also affect other brain regions beyond the epileptic foci. For example, mesial temporal lobe seizures can cause functional and structural abnormalities in the orbitofrontal cortex (Lieb et al., 1991), exacerbating the difficulty in recognizing angry faces in PWE. Numerous non-invasive brain stimulation (NIBS) studies have shown that activation or inhibition of certain brain regions (e.g., temporoparietal junction, ventromedial prefrontal cortex) can affect individuals' recognition abilities for various emotions (Nitsche et al., 2012; Willis et al., 2015; Winker et al., 2018).

However, existing studies have not reached a consensus regarding whether significant differences exist in facial emotion recognition abilities between PWE and healthy individuals. For example, while numerous studies have found that PWE struggle with recognizing fearful faces (Farrant et al., 2005; Laurent et al., 2014; Rainer et al., 2023), some studies suggest that there are no significant differences in facial emotion recognition abilities between PWE and healthy individuals (Banks et al., 2014; Realmuto et al., 2015). This discrepancy may be closely related to the lateralization of epilepsy and the intensity of the emotions involved. Sedda et al. (2013) found that when the emotional intensity of facial expressions is low, right temporal lobe epilepsy patients perform worse than left temporal lobe epilepsy patients, both in overall facial emotion recognition and in recognizing individual emotions. However, when emotional intensity is high, the two groups only differ in overall facial emotion recognition abilities. Therefore, epilepsy seizures may impact both cortical and subcortical pathways involved in facial emotion processing, with right temporal lobe epilepsy patients showing more severe impairment in the cortical pathways. Moreover, epilepsy seizures might affect brain regions sensitive to emotional intensity within the affective-salience network (e.g., ventromedial prefrontal cortex, medial orbitofrontal cortex, and dorsolateral prefrontal cortex) (Metzger et al., 2023), leading to more significant deficits in facial emotion recognition.

The treatment methods for epilepsy also influence facial emotion recognition abilities. Meletti et al. (2009) analyzed the impact of different antiepileptic drugs on facial emotion recognition in temporal lobe epilepsy patients. They found that patients

on phenobarbital performed worse on facial emotion recognition tasks compared to those not taking the drug. This could be directly related to the pharmacological effects of phenobarbital, which enhances GABA receptor activity to inhibit abnormal excitability in the central nervous system. However, prolonged use of this medication may lower central nervous system excitability, affecting cognitive processing, such as facial emotion recognition (Suddock et al., 2024). Moreover, the restorative effects of epilepsy surgery on facial emotion recognition abilities may vary depending on the comparison methods and types of surgery. Most studies use pre- and post-surgery group comparisons to explore this issue (Anderson et al., 2000; Cohn et al., 2015), and the results may be influenced by group differences (e.g., baseline facial emotion recognition abilities) and group effects (Mikula et al., 2021). The type of surgery influences the outcome: anterior temporal lobectomy and selective amygdalohippocampectomy can lead to a decline in facial emotion recognition abilities (Wendling et al., 2015), whereas stereotactic laser thermocoagulation does not have this effect (Drane et al., 2015). Compared to resection surgery, stereotactic surgery avoids damaging neural fiber pathways between the resected regions and other brain areas (Easton & Emery, 2004), thus preventing deficits in facial emotion recognition.

Due to the differences in the maturation and developmental trajectories of the ability to recognize different emotions (Herba & Phillips, 2004; Thomas et al., 2007; Stewart et al., 2019), variations in the age of epilepsy onset may impact patients' facial emotion recognition abilities to varying degrees (Edwards et al., 2017; Qi et al., 2022). The "early-onset" hypothesis suggests that patients with right amygdala damage due to epilepsy onset before the age of 6 will face permanent facial emotion recognition deficits, whereas epilepsy that starts later is less likely to affect the patients' facial emotion recognition abilities (Meletti et al., 2003; Hlobil et al., 2008). This is because accurate facial emotion recognition requires effective integration and transmission of emotional information across various neural structures (Cristinzio et al., 2010). However, earlier onset of epilepsy may impair the efficiency of information transmission between these neural structures, leading to more severe facial emotion recognition deficits in early-onset PWE. Moreover, seizures often accompany feelings of shame (Fiest et al., 2014), which may lead individuals to reduce communication with others, thus hindering the acquisition of experiences related to facial emotion recognition. However, the development of cortical pathways for facial emotion recognition and the enhancement of region-specific brain areas are closely linked to the accumulation of social experience (Leppänen & Nelson, 2006).

7.2. Unanswered Questions and Course for Future Research

Existing studies show that the ability of PWE to recognize facial emotions is influenced by both the lateralization of epilepsy and the intensity of emotions (Meletti et al., 2003; Shaw et al., 2007; Meletti et al., 2009; Sedda et al., 2013; Benuzzi et al., 2014). However, most research focuses on temporal lobe epilepsy, and the mechanisms remain unclear. Future studies should explore the specific patterns of facial emotion recognition in patients with types of epilepsy other than temporal lobe epilepsy and examine the roles of lateralization and emotion intensity. Specifically, future research could investigate the relationship between lateralization and dysfunction in emotion recognition centers (e.g., amygdala, orbitofrontal cortex), especially the neural differences in how different types of epilepsy process various emotions. Since emotion intensity plays a regulatory role in facial emotion recognition (Sedda et al., 2013; Lin et al., 2022), future studies should explore how different intensities of facial emotion stimuli affect the activation of emotional networks in PWE, as well as the interaction between emotion intensity and lateralization, and its combined effect on facial emotion recognition. Comparing neural responses to high and low intensity emotion stimuli will help clarify the role of emotion intensity in facial emotion processing and the neural modulation during processing emotions of different intensities. Additionally, investigating how patients with left- or right-sided epilepsy respond to stimuli of different emotional intensities will shed light on the joint influence of emotion intensity and lateralization on facial emotion recognition pathways. Furthermore, epilepsy may impact cortical and subcortical pathways involved in facial emotion processing, with lateralization playing a significant role. Future studies could use brain imaging to examine cortical and subcortical pathway damage in different lateralized epilepsy groups, providing a theoretical basis for effective interventions.

Gao and Maurer (2009) generated faces with varying emotional intensities (happiness, fear, sadness) to explore facial emotion recognition in healthy children. The results showed significant differences in how children recognized different emotional stimuli. Five-year-olds were able to recognize happy faces at adult levels, even at lower intensities, while their ability to recognize fearful faces did not reach adult levels until the age of ten. Previous research on facial emotion recognition in childhood and adolescence suggests that this ability may vary depending on the emotion category and its intensity. Studies on how brain injury affects specific cognitive functions among different age groups may help clarify the link between brain structure and cognitive processes, providing a foundation for understanding brain mechanisms (Broca, 1861; Gazzaniga & Sperry, 1967). More specifically, tracking changes in facial emotion recognition ability across developmental stages (e.g., childhood, adolescence, early adulthood) in PWE will aid in understanding how emotion type and intensity interact

in the development of recognition abilities and provide important insights into restoring these abilities in PWE.

Moreover, different antiepileptic drugs and types of epilepsy surgery may also affect facial emotion recognition abilities in PWE (Meletti et al., 2009; Wendling et al., 2015; Drane et al., 2015). However, current research has focused less on the effects and mechanisms of epilepsy treatments on facial emotion recognition. Meletti et al. (2009) compared the facial emotion recognition abilities of PWE taking phenobarbital and those not taking it, finding that phenobarbital impaired recognition. However, as 72% of the patients in the study were on multiple antiepileptic drugs, it is unclear whether phenobarbital alone was responsible for the impairment. Therefore, future studies should control the types of antiepileptic drugs used by patients, with clinical permission, to explore how different drugs or combinations affect facial emotion recognition. Machine learning methods, such as support vector machine classification, could also be used to examine the effects of different drugs.

Due to methodological differences and group effects, there is no consensus in past research on whether epilepsy surgery can help restore facial emotion recognition (Yamada et al., 2005; Shaw et al., 2007; Benuzzi et al., 2014; Monti & Meletti, 2015). Additionally, few studies have examined the impact of different types of epilepsy surgery (e.g., resection or stereotactic surgery) on restoring facial emotion recognition. While studies on non-human primates suggest that stereotactic surgery can damage neural cells without affecting fiber pathways (Everitt & Robbins, 1992), no similar findings have been reported in humans. Future research should provide detailed structural and surgical information (e.g., surgical method and site) to help identify the physiological connections underlying facial emotion recognition and offer more scientific and personalized guidance for epilepsy treatment. Moreover, cohort studies that consider the type of surgery, drug combinations, and other factors should be conducted to examine the effects of epilepsy treatments on facial emotion recognition. This will help clarify how treatments influence emotion recognition and provide guidance for the rational use of medications.

8 Conclusion

This review summarizes the impact of factors such as epilepsy type, lateralization characteristics, and age of onset on patients' facial emotion recognition abilities, while also exploring potential mechanisms from a cognitive perspective. However, existing research findings are inconsistent, and further exploration is needed from a multidimensional perspective, particularly regarding the roles of epilepsy lateralization

characteristics, emotion intensity, and treatment methods, especially in terms of dynamic changes at different developmental stages: (1) Epilepsy Lateralization Characteristics. The mechanisms by which lateralization affects facial emotion recognition remain unclear. Future research should focus on the neural differences in patients with different lateralized epilepsy when processing various emotions and, from a developmental perspective, explore how these differences change in children, adolescents, and adults; (2) Emotion Intensity. Emotion intensity significantly affects facial emotion recognition abilities, and its interaction with lateralization characteristics may be stage-specific. Studying the recognition patterns of high and low intensity emotions at different ages in PWE may reveal the neurodevelopmental trajectory of how emotion intensity regulates facial emotion processing; (3) Interaction of Emotion Type and Intensity. Studies on healthy children have shown that the interaction between emotion type and intensity is crucial for the development of facial emotion recognition abilities. However, whether a similar pattern exists in PWE during development remains unclear. Tracking the sensitivity of PWE to the interaction effects of emotion type and intensity at different ages will provide valuable insights into the development of emotion recognition in these patients; (4) Treatment Methods. The long-term impact of antiepileptic drugs and surgical interventions on emotion recognition still requires further investigation. Developmental studies can clarify the potential effects of different treatments on emotion recognition abilities at various stages of development, providing a basis for formulating more individualized treatment strategies.

Overall, future research should adopt a developmental perspective, systematically integrating data on epilepsy lateralization characteristics, emotion intensity, treatment methods, and developmental stages to construct a dynamic model of the mechanisms behind emotion recognition deficits in PWE. This approach will not only deepen our understanding of emotion recognition deficits in PWE but also provide theoretical and practical support for improving their social functioning and promoting psychological development.

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